REMARKS

This Reply, filed in response to the Office Action mailed May 29, 2008, is believed to address all and every issue raised in the Action. A favorable consideration of the application is respectfully requested.

Claim Amendment and Status

Upon entry of the amendment, which is respectfully requested, claims 1-12 will be pending in the application.

In the amendment, claims 11 and 12 are newly added. Support for new claims may be found at, for example, the disclosure of the paragraph bridging pages 21-22.

In the amendment, claims 1, 6, and 9 are amended to improve wording and to more clearly set forth the subject matter defined in the claims. In particular, claims 1 and 6 are amended by incorporating the limitation "wherein the subject is not suffering from diabetes." Support for such amendment can be found in the specification, for example the disclosure at page 2, lines 6-15, page 6, line 11-page 7, line 23, and page 7, line 24-page 8, line 9, where the specification discloses various alternative causes of the overactive bladder and describes status of the art where the compound recited in claims were used for treating diabetes. In this regards, Applicants respectfully submit that the above exclusion limitation is permissible according to MPEP 2173.05(i), which reads:

> Any negative limitation or exclusionary proviso must have basis in the original disclosure. If alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. See *In re Johnson*, 558 F.2d 1008,

> 1019, 194 USPQ 187, 196 (CCPA 1977) ("[the] specification, having described the whole, necessarily described the part remaining."). See also *Ex parte Grasselli*, 231 USPQ 393 (Bd. App. 1983), *aff'd mem.*, 738 F.2d 453 (Fed. Cir. 1984). The mere absence of a positive recitation is not basis for an exclusion. Any claim containing a negative limitation which does not have basis in the original disclosure should be rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Note that a lack of literal basis in the specification for a negative limitation may not be sufficient to establish a *prima facie* case for lack of descriptive support. *Ex parte Parks*, 30 USPQ2d 1234, 1236 (Bd. Pat. App. & Inter. 1993).

Therefore, the amendment excluding subjects suffering from diabetes does not introduce new matter and entry of the amendment is respectfully requested.

Applicants respectfully submit that such amendment is made without prejudice or disclaimer of the scope of the previously presented claims. Applicants reserve their rights to pursue the subject matter included in the previously presented claim, but excluded from the currently presented claim in a separate application.

Formal Matters

Applicants thank the Examiner for acknowledging the claim amendment submitted on February 11, 2008.

Applicants indicate that no sworn English translation of a priority document was submitted and apologize for any confusion.

Applicants further thank the Examiner for considering the Information Disclosure Statement filed on June 12, 2008, however, Applicants indicate that an initialed copy of the PTO/SB/08 form was not attached to the Office Action. Applicants respectfully request a copy.

Response to Maintained Rejections of Non-statutory Obviousness type Double Patenting and 35 U.S.C. § 102(b)

The Office has maintained the previous rejections of non-statutory obviousness-type double patenting (ODP) and under 35 U.S.C. § 102(b). In response to the Applicants' arguments that the cited references do not necessarily teach the claimed invention (because patients with diabetes do not *necessarily* have overactive bladder or drugs suitable for treating diabetes do not necessarily show activities of treating overactive bladder), the Office contends that such argument is not persuasive and again refers to the discussions set forth in the Office Action mailed November 15, 2007.

In addition, the Office indicates that a) Applicant's assertion that it would be counterintuitive to practice the instant claimed method in treating urinary overflow incontinence in patients with diabetes is not supported by any objective evidence, b) there is a clear nexus between bladder overactivity, urinary incontinence, and diabetes as evidenced by the teaching of Cecil (already made of record, pages 23-24, and 637642), and c) the scope of Claims 1-3, and 6-10 exceeds the scope of "urge incontinence."

The Office reiterates the non-statutory ODP and §102(b) rejections based on the disclosure of Maruyama et al. (WO99/20607; equivalent English translation U.S. Patent 6,346,532 B1).

Applicants respectfully traverse the rejections.

Without conceding with or commenting the rejections on the merits, Applicants amend claims 1 and 6 solely in order to advance the prosecution of the application to exclude diabetes patients population, rendering the rejection moot.

Furthermore, Applicants reiterate by incorporating by reference previously presented arguments regarding Maruyama. That is, Maruyama fails to teach the use of the claimed composition in a subject suffering from overactive bladder.

The rejections are believed to be unsustainable and their withdrawal in respectfully requested.

Response to Rejection under 35 U.S.C. § 103

Claims 1-10 are rejected under 103(a) as being unpatentable over Maruyama *et al.* (WO99/20607; equivalent English translation U.S. Patent 6,346,532 B1), in view of Cecil and Fabiano *et al.* (US patent 6,204,285).

The Office relies upon teachings of Maruyama and Cecil for the same reasons discussed in connection with the rejection under 102(b) discussed above.

Fabiano is relied upon to show the general state of the art regarding the use of anticholinergic drugs in treating urinary incontinence. Fabiano allegedly teaches methods of treating urinary incontinence, such as incontinence resulting from bladder detrusor instability, stress incontinence, overflow incontinence, urge incontinence, comprising administering an anticholinergic agent, glycopyrrolate. The Office further relies on the disclosure at col. 1, line 65 to col. 2, line 16 of Fabiano to allege that Fabiano teaches that no treatment for incontinence, including existing drug therapies, has achieved complete success with all classes of incontinent patients, and without significant side effects. The Office's position is that Fabiano identified a

problem existed in the art and thus one skilled in the art would have been motivated to combine the teachings of Maruyama and Cecil to reach the presently claimed invention.

The Office further relies upon and cites Cruz *et al.* (US Patent 6,630,515) and Skolnick (US Patent Application Pub. No. 2008/0009538; post art reference).

Applicants respectfully traverse.

The combined teachings of the reference fails to teach all and every element of currently presented claims. That is, none of the references teach a method of treating a subject suffering from overactive bladder. With respect to the Office's allegation that diabetes population can suffer from overactive bladders and thus the cited references inherently teaches the subject matter defined in the claims, Applicants respectfully submit that the currently presented claim renders such allegation moot, because the currently presented claims excludes the patient population suffering from diabetes.

Applicants further respectfully submit that one skilled in the art were able to determine a subject who is in need of treatment of overactive bladder, but does not suffer from diabetes, in light of the disclosure of the application providing descriptions of the overactive bladder combined with knowledge available in the art at the time of the filing of the application, without undue experiments. In support of the above arguments, Applicants submit copies of the following documents:[1]

[1] Copies of the documents a)-c) are submitted with this Amendment under a separate transmittal letter. The Office is kindly reminded that an IDS is not required to submit references which are relied upon by Applicants in support of their arguments in response to the Office's rejection.

a) Abrams, et al., "The Standardisation of Terminology in Lower Urinary Tract Function: Report From the Standardisation Sub-Committee of the International Continence Society," Urology 61:37-49 (2003), which discloses that diagnosis of overactive bladder has been routinely performed by one skilled in the art;

b) World Health Organization, Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications, WHO (1999), which discloses that diagnosis of diabetes mellitus has been routinely performed by one skilled in the art; and

c) World Health Organization, Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia, WHO/IDF Consultation (2006), which describes the diagnosis standards in 1999 of diabetes mellitus are maintained in 2006.

In addition, Applicants would like to clarify and correct a part of their previous arguments, which contain typographic errors, wherein they indicated that the compound of the present invention is an anticholinergic agent (See page 9, lines 21-22; page 10, lines 19 - 20 of the Amendment filed February 11, 2008). The compound recited in the claims of the present application is an adrenaline β3 receptor agonist and is not an anticholinergic agent. It would have been obvious to one skilled in the art that the compound recited in the claims is not an anticholinergic agent, but is an adrenaline β3 receptor agonist, from the disclosure of the specification and knowledge available in the art at the time of the invention.

The specification of the present application describes that CGP-12,177A, which is a β3 receptor agonist, is known to cause relaxation of the bladder and can be used to treat urinary frequency and urinary incontinence. Page 2, line 17 - page 3, line 4 of the specification. Thus, one skilled in the art would recognize from the description that the compound of the present application which shows bladder relaxation action (as described through Examples), is a β3 receptor agonist. Additionally, as correctly concluded in the above-identified parts of the previously presented arguments in the February 11, 2008 Amendment, Applicants indicate that acontractile bladder from diabetes is described as the general cause of overflow-type urinary urgency and therefore one skilled in the art would have considered the administration of the compound of the present invention, which is a β3 receptor agonist and which may have a relaxation action on the bladder, to worsen the urinary incontinence condition. Same is apparent from the teaching of cited Cecil reference, at Table 119-3 on page 641. Therefore, it is believed that the rejection based on Fabiano on the ground that Fabiano teaches the use of anticholinergic drugs in treating urinary incontinence is rendered moot and its withdrawal is respectfully requested.

Furthermore, Applicants respectfully submit that the compound recited in the claims of the instant application shows unexpectedly superior effects in efficacy when compared to known agent for treating overactive bladder, such as CGP-12,177A, which are an adrenaline β3 receptor agonist. For example, Example 1 of the instant application demonstrates superior effects of the compound of the present invention as an agent for treating overactive bladder, when compared

with CGP-12,177A. More specifically, Applicants indicate that the claimed compound performs at a 270-fold higher activity than that of CGP-12,177A in the comparison of the concentration which shows maximum relaxation in the carbachol contraction antagonizing test and 393-fold higher activity than that of CGP-12,177A in the comparison of the concentration which shows maximum relaxation in the potassium chloride contraction antagonizing test.

As such, it is believed that the rejection of claims 1 and 6 are not sustainable. For the same reasons, claims 2-6 and 7-10, which directly or indirectly refer to claims 1 or 6, are also patentable.

Withdrawal of the rejections and favorable reconsideration of the application are respectfully requested.

CONCLUSION

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number **202-775-7588**.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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